

Amendments To The Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Please cancel claims 12, 13, 16, 21, 22, 25, 27, 36, 37, 39, and 41-50, amend claims 11, 20, 23, 26, 28, 34, and 35, and add new claims 51-56 as follows:

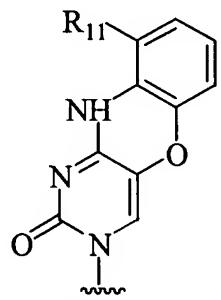
1. (original) A composition comprising a first oligomeric compound and a second oligomeric compound wherein:
 - at least a portion of the first oligomeric compound is capable of hybridizing with at least a portion of the second oligomeric compound;
 - at least a portion of the first oligomeric compound is complementary to and capable of hybridizing to a target nucleic acid; and
 - at least one of the first and the second oligomeric compounds comprises at least one modified nucleoside having enhanced or decreased affinity for the complementary nucleoside in the composition or between the first oligomeric compound and a nucleic acid target; or
 - one of the first and the second oligomeric compounds comprises at least one modified nucleoside having enhanced affinity for the complementary nucleoside in the composition or between the first oligomeric compound and a nucleic acid target and one of the first and the second oligomeric compounds comprises at least one modified nucleoside having decreased affinity for the complementary nucleoside in the composition or between the first oligomeric compound and a nucleic acid target.
2. (original) The composition of claim 1 wherein the first oligomeric compound comprises at least one modified nucleoside having enhanced affinity for the complementary nucleoside in the composition or between the first oligomeric compound and a nucleic acid target and either the first oligomeric compound or second oligomeric compound comprises at least one modified nucleoside having a decreased affinity for the complementary nucleoside in the composition or between the first oligomeric compound and a nucleic acid target.

3. (original) The composition of claim 1 wherein the first oligomeric compound comprises at least one modified nucleoside having a decreased affinity for the complementary nucleoside in the composition or between the first oligomeric compound and a nucleic acid target, and the second oligomeric compound comprises at least one modified nucleotide having an enhanced affinity for the complementary nucleotide in the first oligomeric compound compared to the affinity of an unmodified nucleotide.
4. (original) The composition of claim 1 wherein the second oligomeric compound comprises at least one modified nucleotide having an enhanced affinity for the complementary nucleotide in the first oligomeric compound compared to the affinity of an unmodified nucleotide, and wherein the second oligomeric compound also comprises at least one modified nucleotide having a decreased affinity for the complementary nucleotide in the first oligomeric compound compared to the affinity of an unmodified nucleotide.
5. (original) The composition of claim 1 wherein the at least one modified nucleotide that comprises an enhanced affinity is a nucleotide comprising a nucleotide base modification.
6. (original) The composition of claim 5 wherein the nucleotide base modification comprises a pyrimidine nucleotide comprising a modification at the 2, 4, 5 or 6 position of the pyrimidine nucleotide.
7. (original) The composition of claim 6 wherein the pyrimidine nucleotide comprises a modification at the 2 or 5 position of the pyrimidine nucleotide.
8. (original) The composition of claim 6 wherein the nucleotide base modification comprises a 2-thio U nucleotide substitution for U nucleotide or 2-thio C nucleotide substitution for a C nucleotide.

9. (original) The composition of claim 6 wherein the nucleotide base modification comprises a 5-alkyl, 5-alkenyl, or 5-alkynyl U substitution for a U nucleotide or 5-alkyl, 5-alkenyl, or 5-alkynyl C substitution for a C nucleotide.

10. (original) The composition of claim 6 wherein the nucleotide base modification comprises a 5-methyl U, 5-methyl C, 5-propynyl U, or 5-propynyl C nucleotide.

11. (currently amended) The composition of claim 5 wherein the nucleotide base modification comprises a pyrimidine nucleotide having a modification, wherein the pyrimidine nucleotide is incorporated as one ring of a multiple ring heterocycle, wherein the multiple ring heterocycle further comprises a phenoaxazine moiety, and wherein the multiple ring heterocycle comprises the formula:



wherein:

R₁₁ is (CH₃)₂N-(CH₂)₂-O-; H₂N-(CH₂)₃-; Ph-CH₂-O-C(=O)-N(H)-(CH₂)₃-; H₂N-;
fluorenyl-CH₂-O-C(=O)-N(H)-(CH₂)₃-; phthalimidyl-CH₂-O-C(=O)-N(H)-(CH₂)₃-; Ph-CH₂-O-
C(=O)-N(H)-(CH₂)₂-O-; Ph-CH₂-O-C(=O)-N(H)-(CH₂)₃-O-; (CH₃)₂N-N(H)-(CH₂)₂-O-;
fluorenyl-CH₂-O-C(=O)-N(H)-(CH₂)₂-O-; fluorenyl-CH₂-O-C(=O)-N(H)-(CH₂)₂-O-; H₂N-
(CH₂)₂-O-CH₂-; N₃-(CH₂)₂-O-CH₂-; H₂N-(CH₂)₂-O-, or NH₂C(=NH)NH-.

12-13. (cancelled).

14. (original) The composition of claim 5 wherein the nucleotide base modification comprises a purine nucleotide comprising a modification at the 1, 2, 3, 6, 7 or 8 position of the purine nucleotide.

15. (original) The composition of claim 14 wherein the nucleotide base modification comprises a purine nucleotide comprising a modification at the 2, 6 or 7 positions of the purine nucleotide.

16. (cancelled).

17. (original) The composition of claim 14 wherein the nucleotide base modification comprises a 2,6-diamino purine substitution for an A nucleotide.

18. (original) The composition of claim 1 wherein the at least one modified nucleotide that comprises an enhanced affinity is a nucleotide comprising a nucleotide sugar modification.

19. (original) The composition of claim 18 wherein the nucleotide sugar modification comprise 2'-F, 2'-MOE, 2'-O-methyl, 2'-O-alkyl, 2'-O-alkenyl, 2'-O-alkynyl, 2'-S-alkyl, 2'-S-alkenyl, 2'-S-alkynyl, 2'-amino, 2'-azido, or 2'-allyl.

20. (currently amended) The composition of claim 1 wherein the at least one modified nucleotide that comprises an enhanced affinity is a nucleotide comprising a modified internucleotide linkage, wherein the modified internucleotide linkage comprises a stabilizing internucleotide linkage, and wherein the stabilizing internucleotide linkage comprises a 3'-deoxy-3'-aminophosphoramidate, 3'-deoxy-3'-methylene phosphonate, 3'-deoxy-3'-aminothiophosphoramidate, acetal, thioacetal, amide-3 and amide-4, MMI, hydrazine, or morpholino.

21-22. (cancelled).

23. (currently amended) The composition of claim 1 wherein the at least one modified nucleotide that comprises a decreased affinity is a nucleotide comprising a nucleotide base modification, a nucleotide sugar modification, or at least one modified internucleotide linkage.

24. (original) The composition of claim 23 wherein the nucleotide base modification comprises an inosine nucleotide or a purine ribofuranosyl nucleotide.

25. (cancelled).

26. (currently amended) The composition of ~~claim 25~~ claim 23 wherein the sugar modification comprises a 2'-endo sugar.

27. (cancelled).

28. (currently amended) The composition of ~~claim 27~~ claim 23 wherein the modified internucleotide linkage comprises a destabilizing internucleotide linkage.

29. (original) The composition of claim 28 wherein the destabilizing internucleotide linkage comprises a phosphorothioate, phosphorodithioate, phosphoramidate, phosphotriester, or alkyl phosphonate internucleotide linkage.

30. (currently amended) The composition of claim 5 or ~~claim 23~~ wherein the nucleotide base modification comprises a 2'-substituent group which is, independently, F, -O-CH₂CH₂-O-CH₃, -O-C₁-C₁₂ alkyl, -O-CH₂-CH₂-CH₂-NH₂, -O-(CH₂)₂-O-N(R₁)₂, -O-CH₂C(=O)-N(R₁)₂, -O-(CH₂)₂-O-(CH₂)₂-N(R₁)₂, -O-CH₂-CH₂-CH₂-NHR₁, -O-CF₃, -N₃, -O-CH₂-CH=CH₂, -NHCOR₁, -NH₂, -NHR₁, -N(R₁)₂, -SH, -SR₁, -N(H)OH, -N(H)OR₁, -N(R₁)OH, -N(R₁)OR₁ or -O-CH₂-N(H)-C(=NR₁)(N(R₁)₂);

wherein each R₁ is, independently, H, C₁-C₁₂ alkyl, a protecting group, or substituted or unsubstituted C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, or C₂-C₁₂ alkynyl, wherein the substituent groups are

halogen, hydroxyl, amino, azido, cyano, haloalkyl, alkenyl, alkoxy, thioalkoxy, haloalkoxy, or aryl.

31. (original) The composition of claim 30 wherein each of the 2'-substituent groups is, independently, -F, -O-CH₃, -O-CH₂CH₂-O-CH₃, -O-CH₂-CH=CH₂, -O-CF₃, N₃, NH₂, NHOH, -O-(CH₂)₂-O-N(R₁)₂, -O-CH₂C(O)-N(R₁)₂, -O-CH₂-CH₂-CH₂-NH₂, -O-(CH₂)₂-O-(CH₂)₂-N(R₁)₂ or -O-CH₂-N(H)-C(=NR₁)(N(R₁)₂);

wherein each R₁ is, independently, H, C₁-C₁₂ alkyl, a protecting group, or substituted or unsubstituted C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, or C₂-C₁₂ alkynyl, wherein the substituent groups are halogen, hydroxyl, amino, azido, cyano, haloalkyl, alkenyl, alkoxy, thioalkoxy, haloalkoxy, or aryl.

32. (original) The composition of claim 31 wherein each of the 2'-substituent groups is, independently, -F, -O-CH₂CH₂-O-CH₃, -O-CH₃, -O-CH₂-CH=CH₂, -O-CF₃ or -O-CH₂-CH-CH₂-NH(R_j) where R_j is H or C₁-C₁₀ alkyl.

33. (original) The composition of claim 32 wherein each of the 2'-substituent groups is, independently, F, -O-CH₃, -O-CF₃, or -O-CH₂CH₂-O-CH₃.

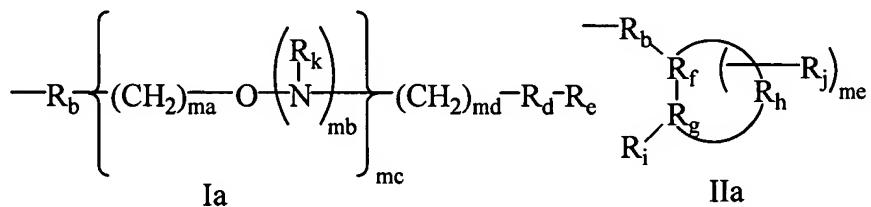
34. (currently amended) The composition of claim 5 or claim 23 wherein at least one modified nucleotide base is a locked nucleic acid (LNA).

35. (currently amended) The composition of claim 18 or claim 25 wherein the nucleotide sugar modification is, independently, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₅-C₂₀ aryl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-alkylamino, -O-alkylalkoxy, -O-alkylaminoalkyl, -O-alkyl imidazole, -OH, -SH, -S-alkyl, -S-alkenyl, -S-alkynyl, -N(H)-alkyl, -N(H)-alkenyl, -N(H)- alkynyl, -N(alkyl)₂, -O-aryl, -S-aryl, -NH-aryl, -O-aralkyl, -S-aralkyl, -N(H)-aralkyl, phthalimido (attached at N), halogen, amino, keto (-C(=O)-Ra), carboxyl (-C(=O)OH), nitro (-NO₂), nitroso (-N=O), cyano (-CN), trifluoromethyl (-CF₃), trifluoromethoxy (-O-CF₃), imidazole, azido (-N₃),

hydrazino (-N(H)-NH₂), aminoxy (-O-NH₂), isocyanato (-N=C=O), sulfoxide (-S(=O)-R_a), sulfone (-S(=O)₂-R_a), disulfide (-S-S-R_a), silyl, heterocyclyl, carbocyclyl, an intercalator, a reporter group, a conjugate group, polyamine, polyamide, polyalkylene glycol, or a polyether of the formula (-O-alkyl)_{ma};

wherein each R_a is, independently, hydrogen, a protecting group, or substituted or unsubstituted alkyl, alkenyl, or alkynyl, wherein the substituent groups are haloalkyl, alkenyl, alkoxy, thioalkoxy, haloalkoxy, aryl, halogen, hydroxyl, amino, azido, carboxy, cyano, nitro, mercapto, a sulfide group, a sulfonyl group, or a sulfoxide group;

or each sugar substituent group has one of formula Ia or IIa:

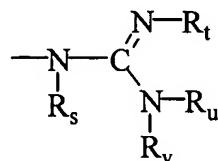


wherein:

R_b is O, S or NH;

R_d is a single bond, O, S or C(=O);

R_e is C₁-C₁₀ alkyl, N(R_k)(R_m), N(R_k)(R_n), N=C(R_p)(R_q), N=C(R_p)(R_r) or has formula IIIa;



IIIa

R_p and R_q are each, independently, hydrogen or C₁-C₁₀ alkyl;

R_r is -R_x-R_y;

each R_s, R_t, R_u and R_v is, independently, hydrogen, C(O)R_w, substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl, substituted or unsubstituted C₂-C₁₀ alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group, or a conjugate group, wherein the substituent groups are hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, or alkynyl;

or, optionally, R_u and R_v, together form a phthalimido moiety with the nitrogen atom to which they are attached;

each R_w is, independently, substituted or unsubstituted C₁-C₁₀ alkyl, trifluoromethyl, cyanoethoxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl, or aryl;

R_x is a bond or a linking moiety;

R_y is a chemical functional group, a conjugate group or a solid support medium;

R_k is hydrogen, a nitrogen protecting group or -R_x-R_y;

each R_m and R_n is, independently, H, a nitrogen protecting group, substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl, substituted or unsubstituted C₂-C₁₀ alkynyl, wherein the substituent groups are hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, alkynyl, NH₃⁺, N(R_u)(R_v), guanidine, or acyl where the acyl is an acid amide or an ester;

or R_m and R_n, together, are a nitrogen protecting group, are joined in a ring structure that optionally includes an additional heteroatom selected from N and O, or are a chemical functional group;

R_i is OR_z, SR_z, or N(R_z)₂;

each R_z is, independently, H, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C(=NH)N(H)R_u, C(=O)N(H)R_u or OC(=O)N(H)R_u;

R_f, R_g and R_h comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms wherein the heteroatoms are oxygen, nitrogen, or sulfur and wherein the ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

R_j is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, N(R_k)(R_m) OR_k, halo, SR_k or CN;

ma is 1 to about 10;

each mb is, independently, 0 or 1;

mc is 0 or an integer from 1 to 10;

md is an integer from 1 to 10;
me is from 0, 1 or 2; and
provided that when mc is 0, md is greater than 1.

36-37. (cancelled).

38. (original) The composition of claim 1 wherein each of the first and second oligomeric compounds comprises from about 12 to about 30 nucleobases.

39. (cancelled).

40. (original) The composition of claim 1 wherein each of the first and second oligomeric compounds comprises from about 19 to about 23 nucleobases.

41-50. (cancelled).

51. (new) The composition of claim 23 wherein the nucleotide base modification comprises a 2'-substituent group which is, independently, F, -O-CH₂CH₂-O-CH₃, -O-C₁-C₁₂ alkyl, -O-CH₂-CH₂-NH₂, -O-(CH₂)₂-O-N(R₁)₂, -O-CH₂C(=O)-N(R₁)₂, -O-(CH₂)₂-O-(CH₂)₂-N(R₁)₂, -O-CH₂-CH₂-CH₂-NHR₁, -O-CF₃, -N₃, -O-CH₂-CH=CH₂, -NHCOR₁, -NH₂, -NHR₁, -N(R₁)₂, -SH, -SR₁, -N(H)OH, -N(H)OR₁, -N(R₁)OH, -N(R₁)OR₁ or -O-CH₂-N(H)-C(=NR₁)(N(R₁)₂);

wherein each R₁ is, independently, H, C₁-C₁₂ alkyl, a protecting group, or substituted or unsubstituted C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, or C₂-C₁₂ alkynyl, wherein the substituent groups are halogen, hydroxyl, amino, azido, cyano, haloalkyl, alkenyl, alkoxy, thioalkoxy, haloalkoxy, or aryl.

52. (new) The composition of claim 51 wherein each of the 2'-substituent groups is, independently, -F, -O-CH₃, -O-CH₂CH₂-O-CH₃, -O-CH₂-CH=CH₂, -O-CF₃, N₃, NH₂, NHOH, -

O-(CH₂)₂-O-N(R₁)₂, -O-CH₂C(O)-N(R₁)₂, -O-CH₂-CH₂-CH₂-NH₂, -O-(CH₂)₂-O-(CH₂)₂-N(R₁)₂ or -O-CH₂-N(H)-C(=NR₁)(N(R₁)₂);

wherein each R₁ is, independently, H, C₁-C₁₂ alkyl, a protecting group, or substituted or unsubstituted C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, or C₂-C₁₂ alkynyl, wherein the substituent groups are halogen, hydroxyl, amino, azido, cyano, haloalkyl, alkenyl, alkoxy, thioalkoxy, haloalkoxy, or aryl.

53. (new) The composition of claim 52 wherein each of the 2'-substituent groups is, independently, -F, -O-CH₂CH₂-O-CH₃, -O-CH₃, -O-CH₂-CH=CH₂, -O-CF₃ or -O-CH₂-CH-CH₂-NH(R_j) where R_j is H or C₁-C₁₀ alkyl.

54. (new) The composition of claim 53 wherein each of the 2'-substituent groups is, independently, F, -O-CH₃, -O-CF₃, or -O-CH₂CH₂-O-CH₃.

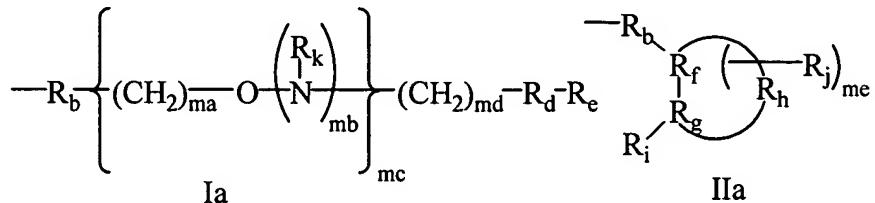
55. (new) The composition of claim 23 wherein at least one modified nucleotide base is a locked nucleic acid (LNA).

56. (new) The composition of claim 23 wherein the nucleotide sugar modification is, independently, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₅-C₂₀ aryl, -O-alkyl, -O-alkenyl, -O-alkynyl, -O-alkylamino, -O-alkylalkoxy, -O-alkylaminoalkyl, -O-alkyl imidazole, -OH, -SH, -S-alkyl, -S-alkenyl, -S-alkynyl, -N(H)-alkyl, -N(H)-alkenyl, -N(H)-alkynyl, -N(alkyl)₂, -O-aryl, -S-aryl, -NH-aryl, -O-aralkyl, -S-aralkyl, -N(H)-aralkyl, phthalimido (attached at N), halogen, amino, keto (-C(=O)-Ra), carboxyl (-C(=O)OH), nitro (-NO₂), nitroso (-N=O), cyano (-CN), trifluoromethyl (-CF₃), trifluoromethoxy (-O-CF₃), imidazole, azido (-N₃), hydrazino (-N(H)-NH₂), amineoxo (-O-NH₂), isocyanato (-N=C=O), sulfoxide (-S(=O)-R_a), sulfone (-S(=O)₂-R_a), disulfide (-S-S-R_a), silyl, heterocyclyl, carbocyclyl, an intercalator, a reporter group, a conjugate group, polyamine, polyamide, polyalkylene glycol, or a polyether of the formula (-O-alkyl)_{ma};

wherein each R_a is, independently, hydrogen, a protecting group, or substituted or unsubstituted alkyl, alkenyl, or alkynyl, wherein the substituent groups are haloalkyl, alkenyl,

alkoxy, thioalkoxy, haloalkoxy, aryl, halogen, hydroxyl, amino, azido, carboxy, cyano, nitro, mercapto, a sulfide group, a sulfonyl group, or a sulfoxide group;

or each sugar substituent group has one of formula Ia or IIa:

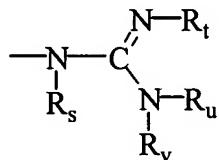


wherein:

R_b is O, S or NH;

R_d is a single bond, O, S or C(=O);

R_e is C_1-C_{10} alkyl, $N(R_k)(R_m)$, $N(R_k)(R_n)$, $N=C(R_p)(R_q)$, $N=C(R_p)(R_r)$ or has formula IIIa;



IIIa

R_p and R_q are each, independently, hydrogen or C₁-C₁₀ alkyl;

R_r is $-R_x - R_y$;

each R_s, R_t, R_u and R_v is, independently, hydrogen, C(O)R_w, substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl, substituted or unsubstituted C₂-C₁₀ alkynyl, alkylsulfonyl, arylsulfonyl, a chemical functional group, or a conjugate group, wherein the substituent groups are hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, or alkynyl;

or, optionally, R_u and R_v , together form a phthalimido moiety with the nitrogen atom to which they are attached;

each R_w is, independently, substituted or unsubstituted C₁-C₁₀ alkyl, trifluoromethyl, cyanoethoxy, methoxy, ethoxy, t-butoxy, allyloxy, 9-fluorenylmethoxy, 2-(trimethylsilyl)-ethoxy, 2,2,2-trichloroethoxy, benzyloxy, butyryl, iso-butyryl, phenyl, or aryl;

R_x is a bond or a linking moiety;

R_y is a chemical functional group, a conjugate group or a solid support medium;

R_k is hydrogen, a nitrogen protecting group or -R_x-R_y;

each R_m and R_n is, independently, H, a nitrogen protecting group, substituted or unsubstituted C₁-C₁₀ alkyl, substituted or unsubstituted C₂-C₁₀ alkenyl, substituted or unsubstituted C₂-C₁₀ alkynyl, wherein the substituent groups are hydroxyl, amino, alkoxy, carboxy, benzyl, phenyl, nitro, thiol, thioalkoxy, halogen, alkyl, aryl, alkenyl, alkynyl, NH3+, N(R_u)(R_v), guanidine, or acyl where the acyl is an acid amide or an ester;

or R_m and R_n, together, are a nitrogen protecting group, are joined in a ring structure that optionally includes an additional heteroatom selected from N and O, or are a chemical functional group;

R_i is OR_z, SR_z, or N(R_z)₂;

each R_z is, independently, H, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C(=NH)N(H)R_u, C(=O)N(H)R_u or OC(=O)N(H)R_u;

R_f, R_g and R_h comprise a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms wherein the heteroatoms are oxygen, nitrogen, or sulfur and wherein the ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;

R_j is alkyl or haloalkyl having 1 to about 10 carbon atoms, alkenyl having 2 to about 10 carbon atoms, alkynyl having 2 to about 10 carbon atoms, aryl having 6 to about 14 carbon atoms, N(R_k)(R_m) OR_k, halo, SR_k or CN;

ma is 1 to about 10;

each mb is, independently, 0 or 1;

mc is 0 or an integer from 1 to 10;

md is an integer from 1 to 10;

me is from 0, 1 or 2; and

provided that when mc is 0, md is greater than 1.